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Preparation of Esters by Reaction of Ammonium Salts with Alcohols[1b]

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A modified esterification procedure by which ammonium salts of organic acids react with alcohols to produce esters and ammonia was investigated. This reaction seems to be generally suitable for the preparation of esters of organic acids. Similarly, reaction of amine salts with alcohols gives ester and amine. This method of esterification may be useful for preparing esters from acid-sensitive alcohols and organic acids as well as for preparing esters of certain fermentation acids.

Ammonium salts of organic acids differ markedly from metallic salts in chemical properties. When heated, ammonium salts are converted into amides, accompanied by dissociation into ammonia and the acid.[3] Ammonium salts have been distilled under vacuum, partial dissociation into an acid salt ($RCOONH_4 \cdot RCOOH$) taking place; the acid salt distilled as a pure compound.[4,5]

Other investigators have reported the reaction of ammonium salts with an excess of formaldehyde to liberate the free acid in quantitative yield,[6] and more recently the reaction of ammonium and substituted ammonium salts with diazomethane to produce the methyl ester and ammonia or amine, respectively,[7] has been reported.

In this paper, we describe another novel reaction of ammonium and amine salts of organic acids, namely, the interaction between these salts and alcohols to produce an ester and ammonia or an amine.

$$RCOONH_4 + R'OH \rightleftarrows RCOOR' + NH_3 + H_2O$$

The reaction bears some resemblance to direct esterification, and from an over-all viewpoint may be considered a direct esterification of ammonium salts with alcohols. This method of producing esters, therefore, may be of interest, particularly where the acidic conditions of conventional esterification are deleterious to the reactants as well as in preparing esters of certain fermentation acids.

As far as we can ascertain, there is no mention in the literature that ammonium salts as such are capable of undergoing an esterification type of reaction. There are many instances in which ammonium salts of organic acids have served as starting material for the preparation of esters, but in each case the organic acid was first liberated by addition of equivalent amounts of a strong mineral acid.

These reactions of ammonium salts are typical reactions of either carboxylic acid (the reactions with diazomethane or alcohols), or of ammonia (the reaction with formaldehyde). Perhaps they may be best explained on the basis of dissociation of the salt into acid and ammonia or amine.

The ammonium salts were esterified by refluxing the mixture of ammonium salt and alcohol under conditions permitting continuous removal of both ammonia and water from the reaction mixture. This was conveniently accomplished by using an entraining agent, which in most cases was the alcohol used in the reaction. When water-soluble alcohols were used toluene or some other suitable solvent was added to serve as an entraining agent. Esterification of amine salts was carried out in the

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(3) C. D. Hurd, "Pyrolysis of Carbon Compounds," A. C. S. Monograph 50, Reinhold Publishing Corp., New York, N. Y., 1929, page 507.

(4) R. Reik, *Monatsh.*, **23**, 1033 (1902).

(5) R. Escales and H. Koepke, *J. prakt. Chem.*, **87**, 258 (1913).

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TABLE I

ESTERIFICATION OF AMMONIUM SALTS

Expt. no.	Reactants: NH_4 salt	Mole	Alcohol	Moles	Temp.,[a] °C.	Time, hr.	Conversion, %: Ester	NH_3	Free acid
1	Acetate	1.0	*n*-Butyl	2.5	118–122	7.5	64	88	23
2	Acetate	1.0	*n*-Hexyl	2.5	142–158	2.5	70	86	18
3	Acetate	0.5	Furfuryl[b]	0.55	103–121	3.0	<20	56	
4	Propionate	1.0	*n*-Butyl	2.5	99–126	2.5	23	92	64
5	2-Ethylhexanoate	1.0	*n*-Butyl	2.5	98–131	3.5	0	94	95
6	Crotonate	1.0	Crotyl[b]	1.0	90–118	8.5	12	80	16
7	Benzoate	1.0	*n*-Amyl	2.0	97–159	14.2	42	80	52
8	Adipate	1.0	*n*-Butyl	4.0	97–139	14.3	50	87	
9	Phthalate	0.5	*n*-Butyl	4.0	95–121	9.5	0[c]	51	
10	Glycolate	1.0	*n*-Butyl	2.5	102–130	6.0	27[d]	45	
11	Glycolate	1.0	2-Methylpentyl	2.5	108–160	4.0	22[d]	52	
12	Glycolate	1.0	3-Heptyl	2.5	111–180	5.8	0	38	
13	Glycolate	1.0	2-Ethylhexyl	2.5	111–182	6.0	68	87	
14	Lactate	1.0	*n*-Butyl	2.5	106–134	7.0	49	87	
15	α-Acetoxypropionate	1.0	*n*-Butyl	2.5	98–146	5.0	19[e]	82	11
16	α-Hydroxyisobutyrate	1.0	*n*-Butyl	2.5	95–133	5.0	14	73	
17	Citrate	0.5[f]	*n*-Butyl	2.5	108–128	6.5	0[f]	12	
18	Salicylate	0.5	Isoamyl	2.2	138–143	5.0	0	80	70–95
19	Control:acetic acid	1.0	*n*-Butyl	1.4	111–121	6.5	67	..	
20	Control:lactamide	1.0	*n*-Butyl	2.5	123–137	8.5	0	3	

[a] Initial and final temperatures of the reaction mixture. [b] Toluene (100–200 ml.) was used as an entraining agent. [c] Phthalimide (100% yield) was obtained. [d] Glycolamide (35% yield) was also formed. [e] 30% conversion to butyl lactate. [f] T. H. Easterfield and W. J. Sell, obtained citrazinic acid upon heating diammonium citrate, *J. Chem. Soc.*, 65, 29 (1894).

same manner. However, the amine produced, being non-volatile, remained in the reaction mixture; water was the only component removed by the entraining agent.

In several instances, conversion to ester was reasonably satisfactory—40 to 70% (Table I) in the case of ammonium acetate, benzoate, adipate, lactate and glycolate. No ester was obtained from ammonium salicylate, citrate, phthalate and 2-ethylhexanoate. In general more than 80% was converted to ammonia, indicating that formation of amide was not an important side reaction. Free acid as well as ester was produced, and in some cases the free acid was the predominating reaction product. Amine salts, particularly those of tertiary amines, appeared equally suitable for the preparation of esters.

The fact that the esterification does not occur through the amide as an intermediate seems to be clearly indicated by the absence of ester and ammonia formation when lactamide was refluxed with butanol under the same conditions which produced butyl lactate from ammonium lactate.

Reaction of ammonium acetate with butyl alcohol seemed to be comparable to the non-catalyzed esterification of acetic acid with butyl alcohol, as shown by comparing Experiments 1 and 19 of Table I. Under approximately the same experimental conditions, substantially identical conversion into ester was obtained.

In general the primary alcohols were better suited for this reaction than the secondary alcohols. The amine salts, except primary aliphatic amine salts, behaved in the same manner as the ammonium salts.

Experimental

Salts.—Ammonium acetate and salicylate and diammonium citrate were commercially available salts. The other salts were prepared by neutralizing the appropriate acid with an equivalent amount of ammonia or an amine.

Esterification of Ammonium Salts.—The esterification procedure was essentially that described for esterification of ammonium acetate with *n*-butyl alcohol. A mixture of 1.0 mole of ammonium acetate, either solid or in a concentrated aqueous solution and 2.5 moles of *n*-butyl alcohol was refluxed in an apparatus conventionally used in esterification reactions to displace the equilibrium by removal of water. The vapors from the refluxing reaction mixture were led through a 2-foot column (1-inch diameter) packed with short lengths of glass tubing and condensed over a modified Dean and Stark water-separating trap. The two-phase condensate collected in the trap, and the upper layer was automatically returned to the reaction flask, and the lower water layer, containing some ammonia, was periodically withdrawn. The non-condensable vapor, mainly ammonia, was led into boric acid solution to absorb the remaining ammonia. A safety trap containing a small amount of water was necessary to prevent the boric acid solution from being drawn back into the reaction flask. Total ammonia was determined by titration of the combined aqueous solutions containing ammonia.[8]

During the reaction, the temperature of the refluxing vapor rose from approximately the boiling point of the alcohol–water azeotrope to the boiling point of the alcohol. Refluxing was continued until the removal of water virtually ceased, which in general required 5 to 10 hours in the esterification reactions employing the lower boiling alcohols.

The temperature of the reaction mixture, when an aqueous solution of the ammonium salt was esterified with butyl alcohol, was approximately 100° initially and rose to a final value in the range 120–150°. Higher temperatures of the reaction mixture resulted when higher boiling alcohols were employed.

When reaction was considered terminated, the ester was isolated from the mixture by distillation in vacuum (Table I, Experiments 1, 2, 4, 5, 6 and 13). In other cases, the reaction mixture was first washed with water or cold dilute alkali prior to distillation.

The esters of acetic and propionic acid distilled azeotropically with the alcohol, and the distillate also contained free acid. In these experiments, the conversion into free acid was determined by titration and conversion into ester by saponification.

The results obtained in the esterification of ammonium

(8) E. C. Wagner, *Ind. Eng. Chem., Anal. Ed.*, 12, 771 (1940).

TABLE II

ESTERIFICATION OF SUBSTITUTED AMMONIUM SALTS

Expt. no.	Reactants: Salt	Mole	Alcohol	Mole	Temp.,[a] °C.	Time, hr.	Conversion, % Ester	Amine
1	Quinoline acetate	1.0	*n*-Butyl	1.0	133–149	3.6	46[b]	...
2	Diamylamine acetate	0.5	*n*-Butyl	0.55	143–168	9.5	32	44
3	Dihexylamine acetate	0.5	Furfuryl[c]	0.55	139–166	17.5	10	58
4	Triamylamine acetate	0.5	*n*-Butyl	0.55	142–165	10.0	62[d]	94
5	Trihexylamine acetate	0.5	Furfuryl[c]	0.55	140–158	24.5	30[e]	90
6	Aniline lactate	1.0	*n*-Hexyl	2.5	119–174	2.0	33	48
7	Decylamine lactate	0.34	*n*-Butyl	0.85	115–158	7.0	0[f]	0[f]
8	Dihexylamine lactate	0.5	*n*-Butyl	1.25	119–155	11.5	40	72
9	Tributylamine lactate	0.5	*n*-Butyl	1.25	110–163	5.5	68	...
10	Triamylamine lactate	0.5	*n*-Butyl	1.25	109–152	5.5	42	...
11	Trihexylamine lactate	0.5	*n*-Butyl	1.25	116–157	11.5	78	72[g]

[a] Initial and final temperatures of the reaction mixture. [b] 39% conversion to acid. [c] Toluene, 75–100 ml., was used as an entraining agent. [d] 22% conversion to free acid. [e] 50% conversion to free acid. [f] 68% conversion to *n*-decyllactamide. [g] Isolated by distillation in nitrogen.

salts of various types of organic acids are summarized in Table I.

Esterification of Amine Salts.—The procedure for esterification of amine salts with alcohols was similar to that described for esterification of ammonium salts. The temperature of the refluxing reaction mixture was generally higher than that for the ammonium salt esterifications. Water was the only component removed from the reaction mixture during esterification; the amines formed during the reaction, being high boiling, remained in the reaction mixture. The ester was isolated by distillation of the reaction mixture in vacuum.

Table II summarizes the esterification of various amine acetates and lactates with butyl and furfuryl alcohols. Excepting Experiments 3 and 7, conversion of amine salt to ester and to amine ranged from 30 to 78 and 44 to 94%, respectively.

2-Methylpentyl glycolate, a new compound, had the following properties: b.p. 66° at 1.2 mm.; $n^{20}D$ 1.4340; d^{20}_4 0.9864.

Anal. Calcd. for $C_8H_{16}O_3$: C, 59.97; H, 10.07; sapn. equiv., 160.2. Found: C, 60.13; H, 10.12; sapn. equiv., 160.7.

2-Ethylhexyl glycolate: The properties of this previously undescribed ester were: b.p. 94° at 2.2 mm.; $n^{20}D$ 1.4400.

Anal. Calcd. for $C_{10}H_{20}O_3$: C, 63.79; H, 10.71; sapn. equiv., 188.3. Found: C, 63.92; H, 10.72; sapn. equiv., 188.7.

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